K010953

JUN - 6 2001

11. 510(k) SUMMARY

510(k) Summary Of Safety And Effectiveness Information Supporting A Substantially Equivalent Determination

CELL-DYN 4000 Multi-Parameter Automated Hematology Analyzer with Immuno T-Cell (CD3/4/8) Assay

Submitter's Information:

Submitter: Abbott Laboratories
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Santa Clara, CA 95054

Contact: John Dean
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Summary Date: March 29, 2001

Device Name and Classification:

Proprietary Name: CELL-DYN 4000 Immuno T-Cell (CD3/4/8) Assay

Common Name: CD 3/4/8 Assay

Classification Name: Automated Differential Cell Counter (864.5220)

Predicate Device: Becton Dickinson (BD) Simultest™ IMK-*Lymphocyte* (as analyzed on BD FACScan Flow Cytometer) (K913192).

The following information, as presented in the Premarket Notification 510(k) for the CELL-DYN 4000 System Hematology Analyzer with Immuno T-Cell (CD3/4/8) Assay constitutes data supporting a substantially equivalent determination.

The methods of determination are those used by the CELL-DYN 4000 System and the Becton Dickinson (BD) Simultest™ IMK-*Lymphocyte* (as analyzed on BD FACScan Flow Cytometer). These methods collectively perform one or more of the determinations which are combined in the CELL-DYN 4000 System with Immuno T-Cell (CD3/4/8) Assay.

Intended Use

The intended use of the CELL-DYN 4000 Immuno T-Cell (CD3/4/8) Assay is to report the count of T-lymphocytes and associated T-Cell subsets in EDTA-anticoagulated human whole blood. The Assay is intended for use on the CELL-DYN 4000 System, a fully automated hematology analyzer. The Assay is intended for *in vitro* diagnostic use in a clinical laboratory of a hospital or medical clinic, a reference laboratory, or a research laboratory.

CELL-DYN® 4000 Immuno T-Cell (CD3/4/8) Assay

The CELL-DYN 4000 System with the Immuno T-Cell (CD3/4/8) Assay is an automated differential cell counter used to identify and classify the following formed elements of the blood:

White Blood Cell Parameters

WBC:	White Blood Cell count
NEU:	Neutrophil absolute count
%N:	Neutrophil percentage of WBCs
LYM:	Lymphocyte absolute count
%L:	Lymphocyte percentage of WBCs
MONO:	Monocyte absolute count
%M:	Monocyte percentage of WBCs
EOS:	Eosinophil absolute count
%E:	Eosinophil percentage of WBCs
BASO:	Basophil absolute count
%B:	Basophil percentage of WBCs
WVF [1]:	WBC Viable Fraction
%CD3 [2]:	Percentage of lymphocytes that are T cells (CD3+ cells)
CD3T:	Absolute number of T lymphocytes (CD3+ cells)
%CD4:	Percentage of lymphocytes that are T-helper/inducer cells (CD3/CD4 positive cells)
CD4T:	Absolute number of T-helper/ inducer lymphocytes (CD3/CD4 positive cells)
%CD8:	Percentage of lymphocytes that are T-suppressor/cytotoxic (CD3/CD8 positive cells)
CD8T:	Absolute number of T-suppressor/ cytotoxic lymphocytes (CD3/CD8 positive cells)
4/8:	Ratio of T-helper/inducer to T-suppressor/cytotoxic lymphocytes (ratio of CD4 positive cells to CD8 positive cells)
v4 [1]	Absolute number of viable T-helper/inducer lymphocytes (CD3/CD4 positive cells)
v8 [1]	Absolute number of viable T-suppressor/cytotoxic lymphocytes (CD8 positive cells)
v4/8 [1]	Ratio of viable T-helper/inducer lymphocytes to viable T-suppressor/ cytotoxic lymphocytes (ratio of viable CD4 positive to viable CD8 positive cells)

Red Blood Cell Parameters

RBC:	Red Blood Cell count
HGB:	Hemoglobin concentration
HCT:	Hematocrit
MCV:	Mean Corpuscular Volume
MCH:	Mean Corpuscular Hemoglobin
MCHC:	Mean Corpuscular Hemoglobin Concentration
RDW:	Red Cell Distribution Width
NRBC:	Nucleated Red Blood Cell absolute count
NR/W:	NRBCs per 100 WBCs
RETC:	Reticulocyte absolute count
%R:	Reticulocyte percentage of RBCs
IRF:	Immature Reticulocyte Fraction

Platelet Parameters

PLT:	Platelet count
MPV:	Mean Platelet Volume
PCT [1]:	Plateletcrit
PDW1:	Platelet Distribution Width
CD61:	CD61 count of platelets
PLTs [1]:	CD61 count of small platelets
PLTe [1]:	CD61 count of large platelets

NOTE: [1] Clinical significance has not been established for this parameter. Therefore, it is not reportable in the USA. It is provided for laboratory use only.

[2] CD indicates Cluster Designation

Device Description

The CELL-DYN 4000 System with Immuno T-Cell (CD3/4/8) Assay is a fully automated, immunology-based method for enumerating T-cells and their helper/inducer and suppressor/cytotoxic subsets in whole blood.

The principles of operation of the assay are:

1. The reagents are two-color, direct immunofluorescence reagents.
2. Anti-CD3 reacts with the CD3/T cell antigen receptor complex found on the majority of normal human peripheral blood lymphocytes.
3. Anti-CD4 reacts with the CD4 antigen expressed on T-helper/inducer cell populations.
4. Anti-CD8 reacts with the CD8 antigen expressed on T-suppressor/cytotoxic cell populations.
5. The anti-CD3 is conjugated with FITC; the anti-CD4 and anti-CD8 are conjugated with PE.

Bound antibody can be detected by fluorescence when illuminated with argon-ion laser light inside the optical flow cell. The T-cell subsets are then enumerated.

The CELL-DYN 4000 System has five main modules:

1. The Analyzer, which aspirates, dilutes, and analyzes each whole blood specimen
2. The Autoloader, which automatically identifies, mixes, and presents specimens for processing
3. The Pneumatic Unit, which controls fluid movement in the analyzer and tube movement in the Autoloader
4. The Data Station, which controls all system processing and provides the primary operator interface within the system
5. The Color Printer, which generates reports automatically or on demand

The CELL-DYN 4000 System is designed to analyze EDTA-anticoagulated blood and report the following hematological parameters. These parameters are discussed more fully in the CELL-DYN 4000 Operator's Manual, **Section 3:** ***Principles of Operation***.

The CELL-DYN 4000 System with Immuno T-Cell (CD3/4/8) Assay is designed to classify the following elements of EDTA-anticoagulated blood. These cellular elements are reported by the CELL-DYN 4000 analyzer as shown in the following table.

Table 2. CELL-DYN 4000 System with Immuno T-Cell (CD3/4/8) Assay

Chartable Page Parameters	Description of parameters on Chartable Page	**Laboratory Use Only Page Parameters**	Description of parameters on Laboratory Use Only Page
Test Selection: CBC + Diff	Complete Blood Count plus differential parameters	Test Selection: CBC + Diff	Same as Chartable Page
%CD3	Percentage of lymphocytes that are T cells (CD3+ cells)	%CD3	Same as Chartable Page
CD3T	Absolute number of T lymphocytes (CD3+ cells)	CD3T	Same as Chartable Page
%CD4	Percentage of lymphocytes that are T-helper/inducer cells (CD3/CD4 positive cells)	%CD4	Same as Chartable Page
CD4T	Absolute number of T-helper/ inducer lymphocytes (CD3/CD4 positive cells)	CD4T	Same as Chartable Page
		v4	Absolute number of viable T-helper/inducer lymphocytes (CD4 positive cells)
%CD8	Percentage of lymphocytes that are T-suppressor/cytotoxic (CD3/CD8 positive cells)	%CD8	Same as Chartable Page
CD8T	Absolute number of T-suppressor/ cytotoxic lymphocytes (CD3/CD8 positive cells)	CD8T	Same as Chartable Page
		v8	Absolute number of viable T-suppressor/cytotoxic lymphocytes (CD8 positive cells)

Note: CD indicates Cluster Designation

Table 2 (continued)

Chartable Page Parameters	Description of parameters on Chartable Page	**Laboratory Use Only Page Parameters**	Description of parameters on Laboratory Use Only Page
4/8	Ratio of T-helper/inducer to T-suppressor/cytotoxic lymphocytes (ratio of CD4 positive cells to CD8 positive cells)	4/8	Same as Chartable Page
		v4/8	Ratio of viable T-helper/ inducer lymphocytes to viable T-suppressor/ cytotoxic lymphocytes (ratio of viable CD4 positive to viable CD8 positive cells)

Note: CD indicates Cluster Designation

Technological Characteristics

The analyzer counts, sizes, and classifies blood cells by the combination of flow cytometry methods: Laser Optical Scatter and Fluorescence, Focused Flow Impedance, and Absorption Spectrophotometry. Optical Scatter and Fluorescence Technology is used to analyze specimens for the Immuno T-Cell (CD3/4/8) Assay. The CELL-DYN 4000 System uses an Argon-ion laser as the optical light source. The Optical Bench detects light in the form of scatter from blood cell surfaces and internal structures, or fluorescent light from specially stained blood cells. Lymphocyte T Cells, and the subsets identified through this assay, tagged with the monoclonal antibodies (mAb), and conjugated to the fluorescent dyes FITC and PE, produce optical light scatter plus green and yellow fluorescence.

For the WBC parameters and NRBCs, whole blood is diluted with a reagent containing a red fluorescent dye. Data are simultaneously collected for four angles (0°, 7°, 90°, and 90°D [depolarized]) of scatter and red fluorescence (FL3) as each cell passes through the laser beam. NRBCs, identified by fluorescence, are excluded automatically from the WBC count.

The Immuno T-Cell (CD3/4/8) Assay utilizes a two tube, two pellet format consisting of a CD3/4 pellet and a CD3/8 pellet. CD3 is conjugated to FITC; CD4 and CD8 are conjugated to PE. The FL1 and FL2 channels of the CELL-DYN 4000 System Optical Bench are used to detect and measure the amount of fluorescence emitted when the samples are processed.

Similarities and Differences

The two systems are similar in that both systems:

1. Provide quantitation of CD3, CD4, and CD8 in EDTA-anticoagulated whole blood specimens
2. Provide a CD4/CD8 (T Helper/T Suppressor) ratio
3. Use an Argon-ion laser and two-color fluorescence
4. Utilize FITC and PC conjugates
5. Use a self-contained microprocessor to provide automated data analysis

The two systems are different in that the CELL-DYN 4000 System Immuno T-Cell (CD3/4/8) Assay:

1. Is fully automated requiring no manual preparation. The predicate device requires manual preparation of blood samples.
2. Can be processed in either random access or batch analysis. The predicate device is batch analysis only.
3. Utilizes a two-reagent panel. The predicate device utilizes a six-reagent panel.
4. Is a self-contained system obtaining all measurement parameters from the CELL-DYN 4000 System. The predicate device requires an external cell counter to provide the absolute lymphocyte count.
5. Measures T-Cells. The predicate device measures T-Cells, B-Cells, and NK-Cells.

The differences noted do not pose new questions of safety and effectiveness.

Table 3. Table of Comparison of Features and Principles of Operation

	Predicate Device - Becton Dickinson (BD) Simultest™ IMK-*Lymphocyte* (as analyzed on BD FACScan Flow Cytometer)	**Submission Device - CELL-DYN 4000 Immuno T-Cell (CD3/4/8) Assay**
Parameter for comparison of equivalence		
Intended Use	Enumerate: CD3, CD3/CD19, CD3/CD4, CD3/CD8, CD3/CD16+56, CD16, and/or CD56	Enumerate: CD3, CD3/CD4, CD3/CD8
Principle of Operation	Enumeration of T lymphocyte subsets using technologies involving monoclonal antibodies, fluorescence, and light scatter	Same
Technology		
Antibody specificity	Anti-CD3: Leu-4 Anti-CD4: Leu3a Anti-CD8: Leu2a	Same
Fluorescence labels	Two color: FITC, PE	Same
Incubation	Outside instrument Ambient conditions	Same
Device Description	Benchtop flow cytometer (analyzer), computer, and software	Same plus Pneumatic Unit and printer
Measurement:		
Fluorescence excitation	Argon-ion laser 488 nm	Same
Emitted light	Split into two photomultipliers	Same
Presentation of cells	Hydrodynamic focusing	Same
Detection	Two-color immunofluorescence plus optical light scatter	Same
Calibration	Not applicable – proportional count only (instrument is calibrated daily)	No additional calibration
Specimen		
Type	Anticoagulated whole blood	Same
Preparation	Manual	Automated

Table 3 (continued)

	Predicate Device - Becton Dickinson (BD) Simultest™ IMK-*Lymphocyte* (as analyzed on BD FACScan Flow Cytometer)	**Submission Device - CELL-DYN 4000 Immuno T-Cell (CD3/4/8) Assay**
Interfering Substances	Previously fixed and stored cells Previously refrigerated samples Samples from patients taking immunosuppressive drugs Blast cells, unlysed or nucleated red blood cells Hemolyzed samples	Lyse-resistant RBCs Platelet clumps Human anti-mouse antibodies Lymphocyte auto-fluorescence Nucleated red blood cells Immunosuppressant therapy (e.g., OKT3, ATGAM)
General Characteristics		
Time to first result	Approximately 45 minutes	Approximately 8 minutes
Number of reagents	6	2

Equivalency Data

The data compiled to support the claim that the CELL-DYN 4000 System Immuno T-Cell (CD3/4/8) Assay is substantially equivalent to the Becton Dickinson (BD) Simultest™ IMK-*Lymphocyte* (as analyzed on BD FACScan Flow Cytometer) software and reagents (K913192) includes: background, accuracy, precision, linearity, and carryover. The data supports the claim that CELL-DYN 4000 System Immuno T-Cell (CD3/4/8) Assay is substantially equivalent to the Becton Dickinson (BD) Simultest™ IMK-*Lymphocyte* (as analyzed on BD FACScan Flow Cytometer) software and reagents (K913192). The data, including accuracy, precision, linearity, and carryover, and showing performance to manufacturer's specifications, is summarized in the data summary in Appendix **16A**.

Conclusion

The CELL-DYN 4000 System Immuno T-Cell (CD3/4/8) Assay demonstrates substantial equivalence to the predicate device.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN - 6 2001

Mr. John Dean
Manager, Regulatory Affairs
Abbott Laboratories
5440 Patrick Henry Drive
Santa Clara, California 95054

Re: K010953
Trade Name: Abbott Laboratories CELL-DYN® 4000 Immuno T-Cell (CD3/4/8) Assay
Regulation Number: 21 CFR § 864.5220
Regulatory Class: II
Product Code: GKZ
Dated: March 29, 2001
Received: March 30, 2001

Dear Mr. Dean:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

13. INDICATIONS for USE STATEMENT

510(k) Number (if known): K 010953

Device Name: CELL-DYN 4000 Immuno T-Cell (CD3/4/8) Assay

Indications for Use:

The CELL-DYN 4000 System with the Immuno T-Cell (CD3/4/8) Assay is an automated differential cell counter used to identify and classify the following formed elements of the blood:

White Blood Cell Parameters

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Indications for Use Statement (continued)

Red Blood Cell Parameters

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NOTE: [1] Clinical significance has not been established for this parameter. Therefore, it is not reportable in the USA. It is provided for laboratory use only.

[2] CD indicates Cluster Designation

Josephine Bautista

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K010953

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

✓ Prescription Use OR Over-The-Counter Use

(Per 21 CFR 801.109) (Optional Format 1-2-96)

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